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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/712,073	11/13/2003	Beth E. Drees	22156.NP	7922

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EXAMINER	
COUNTS, GARY W	
ART UNIT	**PAPER NUMBER**
1641	

MAIL DATE	DELIVERY MODE
06/25/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/712,073	DREES ET AL.	
	Examiner	Art Unit	
	Gary W. Counts	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,32-34 and 38* is/are pending in the application.

4a) Of the above claim(s) *5,6 and 9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7,8,10-15,32-34 and 38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/01/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I claims 1-15, 32-34 and 38 in the reply filed on May 18, 2007 is acknowledged. The traversal is on the ground(s) that the Examiner has made no contention that the inventions of Group I and Group II are in any way "independent". This is not found persuasive because Inventions I and II are not mutually dependent upon each other, as indicated in the restriction requirement the kit can be used in a materially different process. Applicant further argues that the examiner has not met the second burden of showing that examining all claimed inventions in the application would constitute a serious burden. This is not found persuasive because as indicated in the restriction requirement the inventions have acquired a separate status in the art by their different classification, and the search required for one group is not required for the other. Thus, the inventions require different search terms and a different search strategy which creates a burden on the examiner. Further, it is noted that applicant cancelled the claims directed toward Invention II.

The requirement is still deemed proper and is therefore made FINAL.

NOTE: Applicant failed to respond to the species restriction requirement directed to the assay methods as indicated on page 2-3 of the restriction requirement mailed 04/23/07 . During a telephone conversation with Jennifer McCallum, Attorney on June 7, 2007 a provisional election was made to prosecute the species of fluorogenic assay as recited in claims 10 and 11. Thus, claims 5, 6 and 9 have been withdrawn as

being directed toward a non-elected species. Therefore, applicants elected invention consists of claims 1-4, 7, 8, 10-15, 32-34 and 38.

Specification

2. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 32-34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. The factors that must be considered in determining undue experimentation are set forth in *In re W*ands USPTQ2d 14000. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of

working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The instant claims are directed to a method of screening a disease caused alteration of a lipid phosphatase comprising the step of using the lipid phosphates assay method of claim 1 to detect changes in the lipid phosphatase activity in bodily tissue, blood or serum samples. The specification on page 2 under the section entitled background of the invention, the applicant discloses that lipid phosphatases and alterations in their activity levels are implicated in a variety of signaling pathways that are important in regulation of insulin sensitivity and allergic and immune responses, and which are altered in carcinogenesis. The specification on page 8, lines 21-26 discloses that the signaling pathways involving these lipid modifying enzymes are often perturbed in the events leading to disease, particularly in non-insulin dependent diabetes mellitus and cancer. The specification further discloses that the tools developed in the present invention have significant value for research and in diagnostic applications. The specification on page 9, lines 27-29 discloses that the lipid phosphatase assay is a screening method for disease detection, i.e. Cowden's disease, and a molecule for treating such disease by detection of alteration of lipid phosphatase activity. The specification on page 10, lines 13-15 discloses that the lipid phosphatase assay can be used as a screening method for detection of a disease by detection of a predetermined level of the $PI(3,4)P_2$ or $PI(4,5)P_2$ lipid. The applicant has not disclosed how one skilled in the art can use the method of detecting changes in lipid phosphatase activity and correlating these changes to disease detection. The specification does not provide

working examples, controls or standards or guidance on how to determine disease detection by determining changes in lipid phosphatase activity. Further, it is unclear if increases, decreases or the mere presence of lipid phosphatase is indicative of a disease caused alteration of a lipid phosphatase. Such is not seen as sufficient to support the breath of the claims and one skilled in the art cannot practice the claimed invention without undue experimentation, because in order to establish if the product lipid or lipid phosphatase activity is indicate of disease, one skilled in the art would have to know predetermined levels of each different type of product lipid and determine whether an increase or decrease or the presence of the product lipid is indicative of cancer, non-insulin dependent diabetes and Cowden's disease and one skilled would not have a high level of predictability.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-4, 7, 8, 10-15, 32-34 and 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite because the preamble of the claim does not correlate with the body of the claim. The preamble of the claim appears to be directed to an enzyme method by reciting "A lipid phosphatase assay method" however the body of the claim is directed to determining whether product lipid is present in a solution. The body of the claim does not make clear if a sample containing or suspected of containing lipid phosphatase is exposed to the lipid detector protein or the substrate lipid. The

claim does not make clear if the solution contains lipid phosphatase or is suspected of containing lipid phosphates or if the solution is merely a control sample that may contain only a product lipid. Is applicant performing a method to determine lipid phosphatase activity in a sample or does applicant merely intend to detect a product lipid? The claim does not make clear the relationship of the reagents in the method. Method claims should clearly set forth the various method steps in a positive, sequential manner using active tense verbs such as mixing, reacting and detecting. Method claims should also clearly state each component used in the method and the relationship of the various components, and should not be a mere cataloging of parts. The claims should also conclude with a step relating the method result to the purpose of the method, preferably to the purpose as also set forth in the preamble of the claim.

Claim 1 is vague and indefinite because it is unclear what relationship exits between the lipid detector protein and the product lipid or a substrate lipid. Does the detector protein bind to the lipid product or does it come in close proximity of the lipid product to cause some sort of reaction or chemical change? Although the claim recites that the lipid detector protein has a binding specificity for a product lipid, the claim does not positively recite if the detector protein actually binds to the product lipid.

Claim 4 the recitation "other lipid-binding domain" is vague and indefinite. The specification does not provide a definition for the term "other lipid-binding domains" and it is unclear what applicant is referring to.

Claim 12 is vague and indefinite because it is unclear what relationship the additional lipids in the solution have with the substrate lipid, product lipids, lipid detector

protein and enzyme. Do the additional lipids bind to the lipid detector? Are the additional lipids the substrate or product? Do the additional lipids have a function in the assay? It is unclear what applicant is trying to encompass and further it is unclear what the purpose the additional lipids is. Please clarify.

Claim 13 is vague and indefinite because of the use of the acronym "PIPn". Although the term may have art-recognized meanings, it is unclear if applicant intends to claim the prior art definition. The term should be defined in its first instance. Further, the specification does not provide a definition for PIPn.

Claim 13 the recitation "acts on" is vague and indefinite. It is unclear what applicant intends. Does the phosphatase react with PIPn? Does the phosphatase bind PIPn? Further, it is unclear if the lipid phosphatase is selected from the group as recited or if the PIPn is from the group recited in claim 13. It is recommended to delete the recitation "acts on any PIPn and" from the claim.

Claim 32 is vague and indefinite because the preamble of the claim does not correlate with the body of the claim. The preamble of the claim recites " a method for screening a disease caused alteration of a lipid phosphatase. However, the body of the claim merely requires detection of changes in lipid phosphatase activity and does not correlate this detection with a positive screening of the disease.

Claim 32 "disease caused alteration of a lipid phosphatase" is vague and indefinite because it is unclear what alteration or how a lipid phosphatase is altered. The specification does not provide guidance on alterations or provide definitions to provide for a clear understanding of what applicant is trying to encompass.

Claim 32 is vague and indefinite because it is unclear how applicant is "using" the lipid phosphatase assay. Does applicant determine a specific level or amount of product lipid and compare it to a control or standard? Does applicant determine an increase or decrease in phosphatase activity and somehow correlate it with a disease? Does applicant merely determine the presence of a lipid product and somehow determine an alteration has occurred? Please clarify?

Claim 38 is vague and indefinite because it is unclear how the applicant is "using" the lipid phosphatase assay of claim 1 to screen a compound having an enhancing or inhibiting effect. Does the applicant perform further steps along with claim 1 to determine enhancing or inhibiting effect? Does the assay as recited in claim 1 provide information for comparisons to determine an enhancing or inhibiting effect? Are the results of claim 1 compared to a standard or control and a determination of inhibition or enhancement is determined? Please clarify.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

8. Claims 1-4, 7, 10, 11, 14, 15 and 38 are rejected under 35 U.S.C. 102(a) as being anticipated by Dowler et al (WO 02/12276).

Dowler et al disclose methods for detecting or quantifying enzyme activity such as lipid phosphatases (p. 34 & pages 130-135). Dowler et al disclose exposing a

protein that binds specifically to product lipids. Dowler et al discloses that the protein comprise a PH domain which is specific for product lipids (p. 130). Dowler et al disclose exposing the protein (lipid detector protein) comprising the PH domain to substrate lipid and sample and determining if the protein bound to a product lipid. Dowler et al disclose that the PH domain may be in the form of a fusion protein or that the PH domain may be tagged (p.130 & p.132). Dowler et al disclose that prior to contacting that a microtiter plate surface can be coated with lipid substrate that comprises a chromophore (p. 131). Dowler et al disclose that a FRET assay (fluorgenic assay) can be used to determine the enzyme activity. Dowler et al disclose that the substrate lipid can be immobilized or free in solution. Dowler et al disclose that the substrate lipids can be $PI(3,4,5)P_3$ or $PI(4,5)P_2$ and the product lipid PI(4)P (p. 131). Dowler et al disclose that the method may be used to identify modulators of lipid phosphatase activity (p. 34, lines 21-28) by measuring lipid phosphatase activity in the presence and absence of a compound.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dowler et al (WO 02/12276) in view of Goueli et al (US 6,720,162).

See above for the teachings of Dowler et al.

Dowler et al differ from the instant invention in failing to teach the plate is coated with streptavidin.

Goueli et al teaches method for determining lipid phosphatase activity. Goueli et al disclose coating a plate with streptavidin used in assays for lipid phosphatase activity (col 3 & col 9). Goueli et al disclose that this provides for an easy means to separate the products of an enzymatic reaction from unreacted reactant, enzyme and other nonproduct ingredients of a reaction solution (col 2).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate coated streptavidin and biotin systems as taught by Goueli et al into the methods of Dowler et al because Goueli et al teaches that this provides for an easy means to separate the products of an enzymatic reaction from unreacted reactant, enzyme and other nonproduct ingredients of a reaction solution. Further, the use of streptavidin to immobilize reactants of assays is very well known in the art.

13. Claims 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dowler et al in view of Taylor et al (Analytical Biochemistry, 295, 122-126, 2001).

See above for the teachings of Dowler et al.

Dowler et al differs from the instant invention in failing to teach the lipid phosphatase is myotubularin or PTEN. Dowler et al also fails to specifically state that the sample has additional lipids.

Taylor et al disclose assays for determining phosphoinositide phosphatases such as myotubularin and PTEN which act on phosphoitidylinositol phosphates in samples . Taylor et al disclose that the sample can have different lipids. Taylor et al teaches that these enzymes are studied to better understand their role in the synthesis, breakdown, and interconversion of inositiol lipids.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate or determine myotubularin and PTEN activity as taught by Taylor et al into the method of Dowler et al because Dowler et al is generic with respect to the lipid phosphatases to be determined and Taylor et al teaches that

the determination of myotubularin and PTEN which act on phosphoitidylinositol phosphates in samples provides for a better understanding of their role in the synthesis, breakdown, and interconversion of inositiol lipids.

Double Patenting

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. Claims 1-4, 7.8, 10-12, 14 and 15 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-17 of copending Application No. 10/850,833. Although the conflicting claims are not identical, they are not patentably distinct from each other because each teaches assaying a lipid phosphatase by exposing a lipid recognition protein to a sample. Also, both inventions require a lipid substrate and it would have been obvious to one of ordinary skill in the art that the claims of 10/850833 requiring quantifying the lipid product would also encompass the claims of application 10/712,073.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Gary Counts
Examiner
Art Unit 1641

06/14/07
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